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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,824	KOSAL ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to amendments filed on 12/5/03. Applicant has canceled claims 16. Claims 17-21 are new. There are twenty claims pending and twenty under consideration. Claims 1-16 are method of synthesis. This is the second action on the merits. The application concerns a process of preparing the sodium salt of the antibiotic amoxycillin.

Response to Amendment

2. Applicants' amendments overcome the formal objections made in points #2 and #3 of the previous office action. Applicants cancellation of claim 16 renders moot the art rejections made in points #4-#7.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 remain rejected and claims 17 and 19-21 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Ortega ('585, Ref AA). In the passage spanning line 24, column 1 to line 4, column 4. See also claims 1-5 of the reference. The reference teaches the process of preparing the sodium salt of the antibiotic amoxycillin by preparing an amine salt of amoxycillin *in situ* in a two-

solvent mixture. That process is taught generically in lines 40-52, column 1. The salifying agent sodium diethyloxalacetate is taught in line 26, column 1. The solvents are taught in lines 46-52, column 1. Isolation of sodium salt of the antibiotic amoxycillin by precipitation and filtration is taught in lines 2-3, column 2. The reference is silent as to the crystalline nature of the product formed. However, the word "precipitation" and act of isolation by filtration is understood in the organic chemical arts that the solid formed is crystalline and not colloidal. The contrast made in line 4, column 2 of the reference over lyophilization, which produces non-crystalline, glassy material, is noted.

The Applicants claim a process of forming a suspension of an amine salt in one solvent, adding a second solvent to form a homogeneous solution, adding a salifying agent, and isolating the crystalline product. The difference between the claimed and taught processes is the manner in which the amine salt solution is formed in the two-solvent mixture. In Applicants' claims, the second polar solvent is added second after the amine salt is formed. In the reference the second polar solvent is added before the amine salt is formed. Applicants' process is obvious over that taught in the reference because changing the order of steps in a known multi-step process does not make the process unobvious when no unexpected

results occur, *Ex parte Rubin,* 128 USPQ 440, *Cohn et al v. Comr. Pats*. 148 USPQ 486. Thus, claims 1, 2, 6, and 9 are made obvious.

Applicants' claims 3, 7, and 8 add the limitations of specific amine salts and methanol as the polar solvent. Those limitations are found in the reference in 43-44, column 1 and line 51, column 1 respectively. Thus, claims 3, 7, and 8 are also made obvious.

4. Applicants' claims 4 and 5 require that the first solvent be methyl acetate. The reference teaches that the solvent can be acetonitrile, methylene chloride, or 1,2-dichloroethane in lines 46-52, column 1. The difference between Applicants' claims and the teachings of the reference is the solvent employed. No more than routine skill is required for the process chemist to optimize the solvent choice. To quote the Board of Patent Appeals and Interferences *Ex parte Goldschmidt*, 123 USPQ 41 "It is our opinion that it does not amount to invention for the skilled chemist ... to determine ... which specific organic solvent is most suitable". To quote Judge Gajarsa of the U.S. Court of Appeals Federal Circuit in *Eli Lilly & Co. v. Barr Laboratories Inc.* 55 USPQ2d 1609 at 1613, "choosing a suitable recrystallization solvent was well known to one of ordinary skill in the art. In particular, Dr. Elias J. Corey ("Corey"), a Nobel laureate, testified that fluoxetine hydrochloride is "generally quite easy to purify by recrystallization". Corey also

explained that, although it requires some experimentation, selecting a recrystallization solvent is "very straightforward". Further, Barr's expert testified that "in 1974, sometimes the recrystallization of amine hydrochlorides was indeed routine"." In the alternative, the claimed methanol solvent is an obvious homologue of the taught ethanol solvent. Thus, claims 4 and 5 are also made obvious.

5. Applicants' claims 20 and 21 add limitations that the salifying agent be added in a solution made of the two solvent mixture used for the crystallization process. In lines 19-21, column 2 the reference teaches addition of presumably solid salifying agent and that the solid salifying agent is "solubalized in the reaction mixture". The reaction mixture in question is a mixture of methylene chloride and n-propanol, i.e. a two solvent reaction mixture. The difference between the process as claimed and the taught process is the order in which the solution of the salifying agent is made. In the reference the solution of the salifying agent is made *in situ*. As discussed above, changing the order of steps in a known multi-step process does not make the process unobvious when no unexpected results occur, *Ex parte Rubin,* 128 USPQ 440*, Cohn et al v. Comr. Pats*. 148 USPQ 486. Thus, claims 20 and 21 are made obvious.

The various elements of the Ortega ('585) rejection will be discussed together. The Applicants allege unexpected, superior results and point to their experiment 1 in contrast to experiment 8 of the reference. Applicants' experiment 1 gave a 91% yield. The experiment 8 of the reference gave a 74% yield. This is not persuasive for two reasons. Firstly, Applicants' Experiment 1 used a methyl acetate: methanol ratio of 22.5:10, used triethylamine as the organic base, used salifying agent sodium 2-ethylhexanoate, and was done at 0-5°C. The experiment 8 of the reference used a dichloromethane: methanol ratio of 22.5:10, used dicyclohexylamine as the organic base, used salifying agent sodium diethyloxolacetate, and was done at room temperature, presumably 20-25°C. Only the new claim 18 contains all of the limitation of Applicants experiment 1. The temperature and solvent ratios, both of which will affect yield, are simply not addressed by the present claims. It is unclear that the difference in reaction conditions between those present claimed and those taught in the reference are solely responsible for the change in yield.

Secondly, using 399.86 as the formula weight of sodium amoxycillin, one can readily calculate that Experiment 1 of the reference gave an 83% yield and experiments 2-4 gave a 90% yield. While the improvement from 74 to 91% is a

significant improvement, the change from 90 to 91% is a difference in degree.

According the MPEP §716.02

> Allegations of Unexpected Results Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (differences in sedative and anticholinergic effects between prior art and claimed antidepressants were not unexpected). In *In re Waymouth*, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974), the court held that unexpected results for a claimed range as compared with the range disclosed in the prior art had been shown by a demonstration of "a marked improvement, over the results achieved under other ratios, as to be classified as a difference in kind, rather than one of degree." Compare *In re Wagner*, 371 F.2d 877, 884, 152 USPQ 552, 560 (CCPA 1967) (differences in properties cannot be disregarded on the ground they are differences in degree rather than in kind); *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) ("we generally consider a discussion of results in terms of differences in degree' as compared to differences in kind' . . . to have very little meaning in a relevant legal sense")."

6. Claims 1-14 remain rejected and claims 17-21 are newly rejected under 35 U.S.C. 103(a) as obvious over Callander ('958, Ref. AB). The reference teaches the process of preparing the sodium salt of the antibiotic amoxycillin by preparing the diethyl amine salt of amoxycillin *in situ* in a two-solvent mixture. That process is taught specifically in the passage spanning line 44, column 2 to line 21, column 3. The salifying sodium 2-ethylhexanoate agent is taught in line 51, column 2. The alcohol solvents are taught as isopropanol and ethanol in lines 46 and 66,

column 2 respectively. Isolation of sodium salt of the antibiotic amoxycillin by precipitation and filtration is taught in lines 54-55, column 2. The reference describes the product as crystalline in line 46, column 1, line 56, column 1, and line 24, column 2. The Applicant claims a process of forming a suspension of an amine salt in one solvent, adding a second solvent to form a homogeneous solution, adding a salifying agent, and isolating the crystalline product. The difference between the claimed and taught processes is the manner in which the amine salt solution is formed in the two-solvent mixture. In Applicants' claims, the second polar solvent is added second after the amine salt is formed. In the reference the second polar solvent is added before the amine salt is formed. Applicants' process is obvious over that taught in the reference because changing the order of steps in a known multi-step process does not make the process unobvious when no unexpected results occur, *Ex parte Rubin,* 128 USPQ 440, *Cohn et al v. Comr. Pats*. 148 USPQ 486. See also *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is *prima facie* obvious.). Thus, claims 1-3, 6, 7, and 9 are made obvious.

Applicants' claim 10 requires the salifying agent be a sodium salt of an (C1-5) alcohol. Sodium methoxide as such a reagent is taught in lines 3-4, column 2. Thus, claim 10 is also made obvious. Applicants' claim 12 requires the salifying agent to be added in solution. Line 53, column 2 teaches methyl isobutyl ketone to make such a solution. Thus, claim 12 is made obvious.

7. Applicant's claims 4 and 5 require the polar solvent to be methyl acetate. Applicants' claims 8, 11, and 17-22 require that the second alcohol solvent be methanol. The reference teaches amide solvents for the first solvent in lines 58-63, column 1. The teaching of isopropanol and ethanol for the second alcohol solvent were discussed above. The difference between Applicants' claims and the teachings of the reference are the solvents employed. No more than routine skill is required for the process chemist to optimize the solvent choice. To quote the Board of Patent Appeals and Interferences *Ex parte Goldschmidt*, 123 USPQ 41 "It is our opinion that it does not amount to invention for the skilled chemist ... to determine ... which specific organic solvent is most suitable". To quote Judge Gajarsa of the U.S. Court of Appeals Federal Circuit in *Eli Lilly & Co. v. Barr Laboratories Inc.* 55 USPQ2d 1609 at 1613, "choosing a suitable recrystallization solvent was well known to one of ordinary skill in the art. In particular, Dr. Elias J. Corey ("Corey"), a Nobel laureate, testified that fluoxetine hydrochloride is

"generally quite easy to purify by recrystallization". Corey also explained that, although it requires some experimentation, selecting a recrystallization solvent is "very straightforward". Further, Barr's expert testified that "in 1974, sometimes the recrystallization of amine hydrochlorides was indeed routine"." In the alternative, the claimed methanol solvent is an obvious homologue of the taught ethanol solvent. Thus, claims 4, 5, 8, and 11 are made obvious.

8. Applicants' claims 13 and 14 require the salifying agent be added in methanol and ethyl acetate solution. Line 53, column 2 teaches a methyl isobutyl ketone solution of the salifying agent. The difference between the claims and taught process is the solvent used to make this solution. The reasoning is as above and claims 13-14 are made obvious.

9. Applicants' claims 20 and 21 add limitations that the salifying agent be added in a solution made of the two solvent mixture used for the crystallization process. In lines 34-35, lines 51-52, column 2 and lines 3-4, column 3 the reference teaches addition of a salifying agent in methanol or methyl isobutyl ketone solution. The difference between the process as claimed and the taught process is the solvent used to make the solution of salifying reagent. No more than routine skill is required for the process chemist to optimize the solvent choice. The motivation to use the same solvent for the salifying agent as used in the

crystallization would be to simplify the process, lessen the number of solvent to be kept in stock for the process, and to minimize the number of solvent that must be tested for in the final pharmaceutical product. Thus, claims 20 and 21 are made obvious.

The various elements of the Callander ('958) rejection will be discussed together. The Applicants again allege their superior result of 91% yield and point to a 75% yield taught in Example 2 of the reference. This is not persuasive for two reasons. Firstly, Applicants' Experiment 1 used a methyl acetate: methanol ratio of 22.5:10, used triethylamine as the organic base, used salifying agent sodium 2-ethylhexanoate, and was done at 0-5°C. The experiment 2 of the reference used an isopropyl alcohol: DMF ratio of 1200:175, used diethylamine as the organic base, used the same salifying agent sodium diethyloxolacetate, and was done at 5-10°C. Only the new claim 18 contains all of the limitation of Applicants experiment 1. The temperature, base, and solvent ratios, all of which will affect yield, are simply not addressed by the present claims. It is unclear that the difference in reaction conditions between those present claimed and those taught in the reference are solely responsible for the change in yield.

Secondly, Applicants have confused the chemical assay reported in the reference with yield. The reference prepares sodium amoxycillin but presents the

results based on the free acid, lacking the sodium cation. Using 399.86 as the formula weight of sodium amoxycillin, 419.45 as the formula weight of amoxycillin trihydrate, and correcting for the 16.6% of the product weight that is DMF, one can readily calculate that Experiment 2 of the reference gave a 91% yield. This is identical to the yield reported by Applicants.

10. Claims 1-9, 11, 12, and 15 remain rejected and claims 17 and 19-21 are newly rejected under 35 U.S.C. 103(a) as obvious over Corsi (EP 596,262 A1, Ref BA). The reference teaches the process of preparing the sodium salt of the antibiotic amoxycillin by preparing a salt of amoxycillin with "a suitable base" *in situ* in a two-solvent mixture. That process is taught generically in the passage spanning line 34, page 2 to line 7, page 3. The salifying agent sodium 2-ethylhexanoate is taught in line 45, page 2. The base triethyl amine is taught in line 44, page 2. The two solvents are taught as methanol and C_2-C_5 alcohols in line 36, page 2. Isolation of sodium salt of the antibiotic amoxycillin by precipitation and filtration is taught in lines 6-7, column 7. The reference describes the product as "crystals" in line 32, page 6. The Applicants claim a process of forming a suspension of an amine salt in one solvent, adding a second solvent to form a homogeneous solution, adding a salifying agent, and isolating the crystalline product. The difference between the claimed and taught processes is the manner in

which the amine salt solution is formed in the two-solvent mixture. In Applicants' claims, the second polar solvent is added second after the amine salt is formed. In the reference the second polar solvent is added before the amine salt is formed. Applicants' process is obvious over that taught in the reference because changing the order of steps in a known multi-step process does not make the process unobvious when no unexpected results occur, *Ex parte Rubin,* 128 USPQ 440, *Cohn et al v. Comr. Pats*. 148 USPQ 486. Thus, claims 1-3, 6-9, and 11 are made obvious.

11. Applicants claim 12 requires the salifying agent be added in solution. Line 36-37, page 2 teaches methyl acetate to make such a solution. Applicants' claim 15 requires reverse addition of the amine salt to the solution of the salifying agent. That is taught in lines 25-26, page 3 and lines 30-31, page 6. Thus, claims 12 and 15 are made obvious.

12. Applicants' claims 4, 5, and 17, and 19-21 require that the first solvent be methyl acetate. The reference teaches that the solvent is a C_2-C_5 alcohol in line 36, page 2. The difference between Applicants' claims and the teachings of the reference is the solvent employed. No more than routine skill is required for the process chemist to optimize the solvent choice for reasons cited above.

13. Applicants' claims 20 and 21 add limitations that the salifying agent be added in a solution made of the two solvent mixture of methanol and methyl acetate. The reference teaches that the solvent for the solution of salifying agent is a 500:30 mixture of methyl acetate and methanol in lines 22-23, page 3. Thus, claims 20 and 21 are made obvious.

The various elements of the Corsi (EP 596,262 A1) rejection will be discussed together. The Applicants allege unexpected, superior results and point to their experiment 1 in contrast to experiments 1-5 of the reference. Applicants' experiment 1 gave a 91% yield. The experiment 3 of the reference gave an 80.6% yield. This difference in yield is admittedly a difference in kind not in degree. However, this is not persuasive for one reason. Applicants' Experiment 1 used 160 grams of amoxycillin trihydrate, a methyl acetate: methanol ratio of 22.5:10, used triethylamine as the organic base, used salifying agent sodium 2-ethylhexanoate, and was done at 0-5°C. The experiment 3 of the reference used 70 kilograms (437.5 X) of amoxycillin trihydrate, an isopropyl alcohol: methanol ratio of 215:160, used the same triethylamine as the organic base, used the same salifying agent sodium 2-ethylhexanoate, and was done at 0°C. Except for temperature, only the new claim 18 contains all of the limitation of Applicants experiment 1. The scale, temperature, and solvent ratios, all of which will affect yield, are simply not

addressed by the present claims. It is unclear that the difference in reaction conditions between those present claimed and those taught in the reference are solely responsible for the change in yield. According to the MPEP §716.02(d) R-1 Unexpected Results Commensurate in Scope With Claimed Invention

> "Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support". In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) (Claims were directed to a process for removing corrosion at "elevated temperatures" using a certain ion exchange resin (with the exception of claim 8 which recited a temperature in excess of 100C). Appellant demonstrated unexpected results via comparative tests with the prior art ion exchange resin at 110C and 130C. The court affirmed the rejection of claims 1-7 and 9-10 because the term "elevated temperatures" encompassed temperatures as low as 60C where the prior art ion exchange resin was known to perform well. The rejection of claim 8, directed to a temperature in excess of 100C, was reversed.). See also *In re Peterson*, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003) (data showing improved alloy strength with the addition of 2% rhenium did not evidence unexpected results for the entire claimed range of about 1-3% rhenium); *In re Grasselli*, 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983) (Claims were directed to certain catalysts containing an alkali metal. Evidence presented to rebut an obviousness rejection compared catalysts containing sodium with the prior art. The court held this evidence insufficient to rebut the prima facie case because experiments limited to sodium were not commensurate in scope with the claims.).

14. Claims 1-15 remain rejected and claims 17-21 are newly rejected under 35 U.S.C. 103(a) as obvious over Cabre (WO 97/15579 A1, Ref BB). The reference

teaches the process of preparing a crystalline sodium salt of the antibiotic amoxycillin by preparing a salt of amoxycillin with "a suitable amine" *in situ* in ethanol solution. That process is taught generically in the lines 7-17, page 2. The salifying agents are taught in lines 3-8, page 4 including methoxide, ethoxide, and the C-5 carboxylic acid pivalate. Sodium 2-ethylhexanoate is taught in line 1, page 6. The bases triethylamine, diethyl amine, and diisopropylamine are taught in lines 23-25, page 2. The solvent is taught as ethanol in line 4, page 2. Isolation of sodium salt of the antibiotic amoxycillin by filtration is taught in the last line, page 4. The reference describes the product as "crystals" in the same passage. The Applicants claim a process of forming a suspension of an amine salt in one solvent, adding a second solvent to form a homogeneous solution, adding a salifying agent, and isolating the crystalline product. The difference between the claimed and taught processes is Applicants requirement that the process occur in a two-solvent mixture. The teaching to add a second solvent methyl acetate is found in the reference in line 17, page 2. Thus, Applicants' claims 1-7, 9, 10, and 17-19 are anticipated.

15. Applicants' claim 8 requires that the alcohol solvent be methanol. Claim 11 adds the limitation that the salifying agent be sodium 2-ethylhexanoate. The teaching of the salifying agent in the reference was discussed above. The

difference between Applicants' claims and the teachings of the reference are the use of methanol rather than ethanol as taught in the reference. No more than routine skill is required for the process chemist to optimize the solvent choice for reasons cited above. In the alternative, the claimed methanol solvent is an obvious homologue of the taught ethanol solvent. Thus, claims 8, and 11 are made obvious.

16. Applicants claim 12 requires the salifying agent be added in solution. Lines 1-2, page 4 of the reference teach ethanol. Applicants' claims 15 and 22 require reverse addition of the amine salt to the solution of the salifying agent. That is taught in line 2, page 6. Thus, claims 12, 15, and 22 are made obvious.

17. Applicants' claims 13, 14, 21, and 22 require the salifying agent be added in methanol and methyl acetate solution. Line 1, page 6 teaches an ethanol solution of this salifying agent. The difference between the claims and taught process is the solvent used to make this salifying solution. No more than routine skill is required for the process chemist to optimize the solvent choice for reasons cited above. Thus, claims 13 and 14 are made obvious.

The various elements of the Cabre (WO 97/15579 A1) rejection will be discussed together. Applicants made no specific argument concerning this reverence. However, Applicants' experiment 1 gave a 91% yield. The experiment

3 of the reference gave an 86% yield. Applicants' Experiment 1 used a total of 250 grams of amoxycillin in 650 ml of methyl acetate and methanol, used triethylamine as the organic base, used salifying agent sodium 2-ethylhexanoate, and was done at 0-5°C. The experiment 3 of the reference used a total of 20 grams of amoxycillin in 197 ml of ethanol (0.38 X Applicants' concentration), used the same triethylamine as the organic base, used the same salifying agent sodium 2-ethylhexanoate, and the initial was done at 10-12°C. New claim 18 contains the limitation of Applicants base, solvent, and salifying agent but not temperature or concentration. It is unclear that the difference in reaction conditions between those present claimed and those taught in the reference are solely responsible for the change in yield.

Conclusion

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date

of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

20. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact Mukund Shah SPE of 1624 at (571)-272-0674.

Mukund J. Shah

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

TCMcK/me